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Importance of heart rate variability in social phobia and panic disorder patients

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Abstract

Aim: Heart Rate Variability (HRV) is a simple and noninvasive method for measuring beat-to-beat changes in heart rate, quantified as a periodic variation in RR intervals. The association between anxiety disorders and sudden cardiac death has long been recognized and studied. In this study, the relationship between anxiety disorders and HRV was investigated.

Material and Methods: The study included 93 participants (33 with panic disorder, 25 with social phobia, and 35 controls). Psychiatric evaluation was performed using the Structured Interview Guide (SCID-I), and patient groups were formed. Groups were compared according to SDNN, SDANN, NN50, %pNN50, and RMSSD data.

Results: The mean SDNN values were statistically significantly lower in the panic disorder group than in the other groups (p=0.029 vs the social phobia group and p<0.001 vs the control group). There was no statistically significant difference between the study groups according to the average SDANN, RMSSD, and pNN50 values (p=0.065, p=0.548, and p=0.949, respectively). There was no significant difference between the social phobia group and the control group in terms of any parameter showing heart rate variability.

Discussion: The results of our study suggest that heart rate variability parameters are decreased in patients with panic disorder compared to the control group and that these patients should be evaluated more carefully in terms of sudden cardiac death and other cardiac events.

Keywords

Anxiety Disorder, Heart Rate Variability, Panic Disorder, Social Phobia

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Introduction

Heart Rate Variability (HRV) is the beat-to-beat variation in heart rate, measured as the periodic variation in RR intervals, and is a simple and non-invasive method to assess sympathovagal balance at the sinoatrial (SA) level [1]. HRV is considered a measure of cardiac autonomic tone and an indicator of the cardiorespiratory system because it provides information about sympathetic and parasympathetic balance. HRV is used to objectively assess cardiovascular dysfunction and to determine sympathetic and parasympathetic effects on cardiovascular activity [2].

Sudden death is more common in individuals with anxiety disorders compared to healthy individuals. It has been shown that parasympathetic activity is suppressed, and sympathetic activity is increased in anxiety disorders, especially in panic disorder. This results in a decrease in high-frequency heart rate variability in these patients. Individuals with high levels of anxiety have a 4,5 to 6 times higher risk of sudden cardiac death compared to individuals without anxiety. This increased risk of sudden cardiac death is attributed to abnormal sympathovagal balance [3-5]. This decrease in high-frequency heart rate variability is associated with sudden cardiac death [4].

This study aims to compare the heart rate variability in patients diagnosed with social phobia and panic disorder presenting to the psychiatry outpatient clinic with anxiety complaints against healthy individuals.

Material and Methods

Working Groups and Work Plan

In the study, 33 patients diagnosed with panic disorder and 25 patients diagnosed with social phobia who applied to the psychiatry outpatient clinic of our hospital between May 25, 2012, and December 31, 2012, were evaluated. A control group of 35 people who applied to the check-up outpatient clinic and did not have any health problems was formed. Patients aged between 18 and 60 years who were literate enough to understand and respond to self-reported charts and scales, who did not have hearing or visual impairments that would make understanding and comprehension difficult, and who did not have cognitive impairments due to dementia, psychosis, or mental retardation were included in the study. Patients with any cardiac conditions, such as heart failure, valvular heart disease, coronary artery disease, and palpitations, were excluded. Consent was obtained from all patients for the study.

Heart Rate Variability Analysis

To evaluate the heart rate variability of patients in all groups, 24-hour Holter electrocardiography data were assessed using a Holter device with four leads (DMS 300-4A, MTM Multitechmed GmbH, Hunfelden-Dauborn, Germany) and Cardioscan II Premier software. For HRV analysis, heart recordings of all patients were manually evaluated to exclude artifacts. HRV parameters were determined automatically with a Holter data processing program. The time- and frequency-dependent automatic analysis method was used to determine the mean NN (cycle length between two normal beats), SDNN (standard deviation of all NN intervals throughout the examination), SDNN index (mean of standard deviations of all NN intervals in 5-minute recordings), SDANN (standard deviation of the average NN intervals in 5-minute recordings throughout the study period), NN50 (number of neighboring NN intervals with more than 50 msec difference between them during the entire recording), % pNN50 (number of NN50 divided by the total number of all NNs), and RMSSD (square root of the sum of squares of the differences of consecutive NN intervals in a 24-hour recording) parameters [6, 7].

Laboratory Analysis

Biochemical tests and complete blood counts were performed using fully automatic analyzers. Results were specified separately for each parameter.

Psychiatric Evaluation

The sociodemographic information form was filled out by the researcher, and psychiatric evaluation was performed using the Structured Interview Guide (SCID-I). The Hamilton Anxiety Rating Scale and Hamilton Depression Rating Scale were evaluated by the researcher. Self-reported Panic Agoraphobia Scale (PAAS), Hospital Anxiety and Depression Scale (HAD), State-Trait Anxiety Inventory (STAI 1-2), Bodily Sensation Exaggeration Scale (BDAQ), Anxiety Sensitivity Index-3 (ADI), and Liebowitz Symptoms of Social Phobia Scale (LSFPS) were administered to all participants. Groups were formed as a result of the psychiatric evaluation [8-10].

Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) for Windows 15.0 software. Categorical variables were expressed as number (n) and percentage (%) and analyzed using the Chi-square test (and/or Fisher's exact test). Numerical variables were expressed as mean ± standard deviation, and Student's t-test was used to compare the means of two independent groups. A value of $p < 0.05$ was considered statistically significant for all results.

Ethical Approval

This study was approved by the Ethics Committee of Abant Izzet Baysal University Faculty of Medicine Education, Planning, and Coordination Board (Date: 2012-08-09, No: 2012/13).

Results

A total of 33 patients with panic disorder, 25 patients with social phobia, and 35 patients in the control group were included in the study. Demographic data of the patients are summarized in Table 1. According to the data obtained, no difference was found between the groups in terms of gender, age, and smoking ($p = 0.311$, $p = 0.756$, and $p = 0.424$, respectively). The analysis of laboratory data of the patients is presented in Table 2. According to these data, there was no difference between the groups in terms of hemoglobin, electrolyte levels, thyroid function tests, glucose, and vitamin B12 levels ($p > 0.05$ for all data). The results of the parameters showing heart rate variability between groups are provided in Table 3. According

Table 1. Demographic Characteristics of Patients

	Panic Disorder Group (n=33)	Social Phobia Group (n=25)	Control (n=35)	p
Gender (M/F)	11.22	10/15	18/17	0.311
Age (year)	32.75±10.65	33.04±4.59	28.14±4.33	0.756
Smoking	12 (36%)	5 (20%)	10 (30%)	0.424

Table 2. Comparison of patient groups according to laboratory parameters

Parameters	Panic Disorder Group (n=33)	Social Phobia Group (n=25)	Control (n=35)	p
Haemoglobin (g/dL)	14.13±1.56	13.98±1.38	13.91±1.44	0.862
Sodium	139.53±10.20	137.72±1.53	138.40±4.25	0.853
Potassium	4.21±0.39	4.00±0.23	4.15±0.30	0.056
TSH	1.66±1.00	1.97±0.90	1.81±0.85	0.160
Free T3	3.41±0.98	3.57±0.61	3.40±0.74	0.924
Free T4	1.12±0.12	1.15±0.21	1.11±0.14	0.831
Glucose	90.72±9.27	83.00±12.62	88.12±10.05	0.082
Vitamine B12	308.62±173.96	310.23±172.60	312.15±160.40	0.916

(Abb.; TSH: thyroid stimulating hormone)

Table 3. Comparison of patient groups according to heart rate variability parameters

Parameters	Panic Disorder Group (n=33)	Social Phobia Group (n=25)	Control (n=35)
Minimum Heart Rate	46,8±5,4	46,7±7,1	44,4±12,2
Maximum Heart Rate	171,0±31,9	175,2±44,2	165,0±36,7
Average Heart Rate	76,6±6,4	79,6±8,2	78,6±7,9
SDNN	121,0±31,9*#	142,6±28,5	151,0±32,6
SDANN	103,2±31,4x	121,2±25,6	124,2±30,9
RMSSD	43,4±22,6y	50,2±21,7	61,7±27,8
pNN50	11,8±13,8z	12,8±8,9	19,8±12,1

(Abb; SDNN: Standard deviation of NN intervals, SDANN: Standard deviation of the average NN intervals for each 5 min segment of a 24 h HRV recording, RMSSD: Root mean square of successive RR interval differences, pNN50: Percentage of successive RR intervals that differ by more than 50 ms)
*p=0.029 vs Social Phobia Group; #p<0.001, xp=0.013, yp=0.008, and zp=0.020 vs control group

to the data obtained, there was no difference between the groups in terms of minimum heart rate, maximum heart rate, and average heart rate results (p = 0.658, p = 0.201, and p = 0.508, respectively). The mean SDNN values were statistically significantly lower in the panic disorder group than in the other groups (p = 0.029 vs the social phobia group and p < 0.001 vs the control group). There was no statistically significant difference between the study groups according to the average of SDANN, RMSSD, and pNN50 values (p = 0.065, p = 0.548, and p = 0.949, respectively). However, the mean of these values was statistically significantly lower in the panic disorder group than in the control group (p = 0.013, p = 0.008, and p = 0.020, respectively). There was no significant difference between the social phobia group and the control group in terms of any parameter indicating heart rate variability.

Discussion

In this study, heart rate variability in patients diagnosed with social phobia and panic disorder who applied to the psychiatric outpatient clinic with anxiety complaints was compared with healthy individuals. Especially in patients with panic disorder, there was a significant difference in heart rate variability compared to the control group.

Findings related to cardiovascular abnormality have been known since the first studies on individuals with so-called irritable hearts in the 1870s. Publications on tachycardia and palpitations associated with severe fear and anxiety have made cardiovascular activity the focus of research [3]. It is known that an autonomic nervous system imbalance in the form of increased sympathetic activity affects cardiac electrophysiology and causes ventricular arrhythmias and sudden cardiac death. Neural remodeling in the heart affected by various diseases causes these imbalances in autonomic activity. Heart rate variability, which is an indirect indicator of tonic autonomic interactions at the sinus node level, is used as an indicator of neural control [4].

It is known that there is a close relationship between anxiety disorders and sudden death. Many complex physiological events occurring in acute anxiety states contribute to the occurrence of sudden death. In cases of persistent anxiety, the development of atherosclerosis is accelerated, and sudden death can be triggered. The acute effects of psychological stress leading to sudden death are summarized as causing myocardial ischemia, initiating arrhythmia, activating platelets, and increasing blood viscosity [11]. HRV, defined as frequency changes in sinus node velocity over time, is considered a measure of cardiac autonomic tone and an indicator of the cardiorespiratory system because it provides information about sympathetic and parasympathetic balance [3].

In the measurement of HRV, two measurement parameters are used as time and frequency dependent. In time-dependent measurement, SDNN (standard deviation of normal heartbeats), SDANN (standard deviation of the mean N-N intervals), SDNNI (mean of the standard deviation of all N-N intervals), RMSSD (square root of the mean of the sum of the squares of the differences between neighboring NNs), and pNN50 (obtained by dividing the number of N-Ns by NN50) (10). In frequency-dependent measurements, three main components are defined as very low frequency (VLF) (<0.04 Hz), low frequency (LF) (0.04-0.15 Hz), and high frequency (HF) (0.15-0.40 Hz) [6, 7].

HRV values are an important determinant of mortality after myocardial infarction. Kleigler et al. is one of the first studies showing that a decrease in the SDNN value is closely related to increased mortality [12]. In the ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) study conducted in patients under 80 years of age and eligible for exercise testing, it was shown that SDNN <70, which is an indicator of parasympathetic-sympathetic imbalance, is an important independent predictor of cardiovascular mortality in patients [13]. During psychological stress in patients with anxiety disorders, a decrease in heart rate variability has been found, indicating parasympathetic inhibition. In patients with anxiety

disorders, findings such as stress causing a more inadequate autonomic response, sometimes taking a long time for the autonomic changes to recover, and decreased heart rate variability are considered a serious risk for early mortality [14]. In a study conducted on 2059 patients, it was measured that SDNN and RSA [respiratory sinus arrhythmia] values of patients with anxiety disorder were significantly lower when compared with the control group. These values were found to be similar among the three types of anxiety disorder [14].

In our study, mean SDNN values were statistically significantly lower in the panic disorder group compared to the other groups ($p = 0.029$ vs the social phobia group and $p < 0.001$ vs the control group). There was no statistically significant difference between the study groups according to the mean SDANN, RMSSD, and pNN50 values ($p = 0.065$, $p = 0.548$, and $p = 0.949$, respectively). However, the mean of these values was statistically significantly lower in the panic disorder group than in the control group ($p = 0.013$, $p = 0.008$, and $p = 0.020$, respectively). There was no significant difference between the social phobia group and the control group in terms of any parameter indicating heart rate variability.

Conclusion

Our study found that HRV parameters were statistically significantly lower in patients with panic disorder compared to the control group. These patients should be followed up more closely in terms of cardiac risk since the risk of sudden cardiac death and cardiac events increases as a result of the impaired balance of parasympathetic and sympathetic activity.

Limitation

If this study is conducted in larger study groups, more significant results can be obtained. Also, the inclusion of arrhythmia patients may reveal new results. Additionally, there were no mortal patients in our study. It would be more useful to include this data in a larger series.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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